Black Widow Spider Bite: A Case Study

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Abstract:

This article is a case study of a patient cared for in the hours before her death. After the patient's death, we learned the patient died of a black widow spider bite. This article sheds light on the potential seriousness of this venom and allows for more rapid detection and treatment of those who are unfortunate enough to be bitten. The authors have documented the sequence of events for the patient, outlined the care the patient received, examined the pathophysiology of the body to a spider bite, and then made a passionate appeal for other nurses who work in critical care to do the same with patients in similar situations.

Keywords: Black widow spider bites | Streptococcus pyogenes | venomous bites

Article:

A 56-year-old woman ("Pam") admitted to the medical-surgical intensive care unit (ICU) died within hours of admission despite aggressive treatment. One of the authors, Kristine, discovered after the patient died that she had been bitten by a black widow spider the day before. This article examines the physiological effects of black widow spider bites and the way the patient's treatment might have differed had the team known of the bite. The article examines the progression of the toxic effects of the black widow spider bite, the clinical manifestations to look for, and ways to recognize and treat a patient with a bite. Our aim was to help ICU nurses and physicians recognize these manifestations and institute the treatment needed for a spider bite.

We also hope that ICU nurses will remember a patient whose own dramatic story played out for them in much the same way as this one did for the authors and see the importance of looking deeper into a patient's history upon arrival. Other nurses, we hope, will question the mysterious

and elusive and see the importance of rapid treatment and the deleterious effects of delayed treatment.

THE CASE STUDY

Kristine reported to work for her night shift at 6:45 PM on a spring evening in early May. She would soon discover that it was to be another busy night shift in the 16-bed medical-surgical ICU. Kristine was assigned to be the charge nurse that night, and she had 1 patient and the first admission. Around 8:00 PM, she received word that the unit would be receiving a patient from our sister hospital who would need continuous venovenous renal replacement therapy (CRRT). Our unit was the unit that preformed the majority of CRRTs in our system.

Kristine proceeded to prepare the available room for the admission, to prepare the CRRT machine, and to make certain that all of the necessary supplies were ready. At 10:55 PM, Kristine received report from the primary nurse for the patient, Pam, at the sending hospital. Kristine knew this would be a very long night.

The patient Kristine would be receiving was a 56-year-old woman whose only prior medical history was hypothyroidism, depression, and right-shoulder surgery in 2005. Pam had been working in her yard the prior evening. Around 8:00 PM, she recalled receiving a bite or sting to her right upper arm. Later that night, around 10:00 PM, she noticed that the pain in her right arm had become more intense. She also noticed a round area that was raised and red/bruised looking. She developed nausea and vomiting that continued throughout the night. Throughout the night, she also became more lethargic and had more pain in her arm. The decision was made to call 911 the following afternoon.

At 2:08 PM, the Emergency Medical Services (EMS) crew arrived. During her transport to the hospital, her vital signs were slightly elevated, with her heart rate at 104 beats per minute (bpm), respiratory rate at 20 breaths per minutes, and blood pressure at 128/90 mm Hg in a semi-Fowler's position, and oxygen saturation at 99%. The EMS crew applied an adult nonrebreather mask and a cardiac monitor. A 20-gauge antecubital intravenous line (IV) was inserted, and a 250-mL bolus of normal saline was given. Pam was reported to have a Glasgow Coma Scale score of 15 with normal lung sounds. She was speaking in full sentences normally, and her respirations were regular and normal. Her skin was warm and dry, and her pulse was strong and regular. There was no jugular venous distention, and her pupils were equal and reactive. She was transported to the closest facility for evaluation. Table 1 outlines the sequence of events as they occurred.

Table 1. The Sequence of Events

8:00 PM	Bite or sting to right upper arm
10:00	More intense pain, and a raised, red/bruised looking area noticed. Developed nausea

PM	and vomiting, which continued throughout the night
1:51 PM	911 was called
2:00 PM	EMS arrived on scene
2:08 PM	Patient in ambulance. Vital signs: HR, 104; RR, 20; BP, 128/90; O2 sat 99% on nonrebreather in a semi-Fowler position; 20-gauge IV inserted and a 250-mL bolus of NS was given. GCS = 15, lung sounds - normal, speaking in full sentences, respirations regular, skin W & D, pulse strong & regular, no JVD, and PERL
2:32 PM	Arrived at ED, bruising noted to right arm, pain 7/10, SOB, speaking in short phrases/words, hyperventilating, skin was dusky, A & O x 3, ‘‘entire right elbow area exhibits dark ecchymotic-type discoloration’’
2:45 PM	Rectal temperature, 100.8; RR, 18 breaths/min; O2 sat 98% on room air, cyanotic finger tips and lips
2:57 PM	IV infiltrated during ceftriaxone (Rocephin) infusion, D/C’d. Unsuccessful 2nd IV site attempt. Second attempt at IV site successful and Rocephin completed.
2:58 PM	BP, 110/68 supine
3:00 PM	Chest x-ray done and ECG done
3:04 PM	Seen by critical care team. Diagnosed with ARDS and septic shock. RIJ CVC inserted
3:30 PM	Cool, clammy, diaphoretic, peripheral cyanosis, BP undetectable. Patient states ‘‘I feel worse, I feel more lethargic.’’ Given NS wide open. Foley catheter placed
4:50 PM	Received 50 mg fentanyl and 2 mg midazolam (Versed)
4:54 PM	Received 2 mg Versed. ‘‘Arms and legs kept getting colder and colder. Unable to draw labs here due to patient’s condition, to be drawn in ICU. Unable to obtain a BP or pulse ox’’
4:57 PM	Fentanyl 50 mg given and #8 ETT placed. ‘‘Patient began to pink up some, and extremities began to warm up’’
5:15 PM	Transported to ICU where verbal report was given
5:50 PM	Seen by general surgery and infectious disease physician
6:02 PM	Femoral arterial catheter placed by critical care NP. Poor blood flow and poor BP tracing noted
7:30 PM	Bronchoalveolar lavage done by respiratory care
8:00 PM	Seen by renal physician
8:00 PM	Has the following meds infusing: vasopressin, Neo-Synephrine, Levophed with NS, sodium bicarbonate, Versed, NS. Also received 103 mL albumin. Bleeding noted at RIJ and sclera
10:55 PM	Report given to receiving nurse, patient transferred to stretcher

11:00 PM	Received patient from transport team
12:30 AM	Left femoral double-lumen hemodialysis catheter placed by renal MD
12:53 AM	Code blue called
1:12 AM	Pronounced dead

Abbreviations: A & O, alert and oriented; ARDS, adult respiratory distress syndrome; BP, blood pressure; CVC, central venous catheter; D/C, discharge; ECG, electrocardiogram; ED, emergency department; ETT, endotracheal tube; GCS, Glasgow Coma Scale; HR, heart rate; ICU, intensive care unit; IV, intravenous; JVD, jugular venous distension; NP, nurse practitioner; NS, normal saline; O2 sat, oxygen saturation; Ox, oximetry; PERL, pupils equal and reactive to light; RIJ, right internal jugular; RR, respiratory rate; SOB, shortness of breath; W & D, warm and dry.

Kristine remembers Pam's arrival on the unit as if it was yesterday. The critical care transport team came running into the unit at 10:55 PM. There were 3 of them, all red faced, sweating, and out of breath. Their urgency could be seen on their faces. There were multiple IV bags and blood infusing via 4 different pumps hitting against each other from the swinging caused by the rapid movement of the stretcher. One of the crew was breathing for the patient with a bag valve mask. The cardiac monitor was sitting between her legs. Underneath all of the tubes, wires, pumps, cardiac monitor, and people, Pam's face and 2 arms were barely visible.

As the crew rushed into the waiting arms of 5 medical-surgical ICU nurses, a respiratory therapist, and a nurse technician, the process of transferring patient information, equipment, supplies, and ultimately the patient began. What at first glance might seem a daunting and time-consuming task to unravel proved to be a smooth, seamless, and rapid transition because of the efforts of everyone working in harmony toward one common goal: to help Pam. The primary nurse for the transport apologized for not calling with a report saying he was not able to because of the patient's unstable condition. Kristine reassured him that she understood and told him not to worry. He proceeded to give Kristine a verbal bedside report as the team worked to transfer Pam.

The team immediately notified the physician of Pam's arrival on the unit via the video remote physician monitoring system. Within seconds, the physician was viewing everything that was happening in the room. He continued providing orders and direction throughout the night. Table 2 provides a timeline of these orders. We also notified the renal physician of Pam's arrival. Pam had a dusky, cyanotic color and was cold to the touch. She did not respond to any verbal, tactile, or painful stimuli. Her pupils were small and very sluggish, her scleras were bloody, and she had conjunctival edema. There was a necrotic-appearing area on the inner aspect of the right upper arm that was oval and approximately 23 cm long and 14 cm wide.

Table 2. Laboratory Values

WBC	5:32 PM = 8.2, 6:30 PM = 9.2 (4.0-10.5 μL)
RBC	5:32 PM = 5.61H, 6:30 PM = 4.96 (3.87-5.11 μL)
HGB	5:32 PM = 16.4, 6:30 PM = 14.4 (0-15.0 g/dL)
HCT	5:32 PM-50.5, 6:30 PM = 44.5 (36.0-46.0%)
PLT	5:32 PM = 152, 6:30 PM = 141 L (150-400 μL)
PH (7.35-7.45)	5:45 PM = 6.98, 8:04 PM = 7.15, 9:34 PM = 7.22 mm Hg
Pco_2 (35.0-45.0)	5:45 PM = 41.1, 8:04 PM = 43.3, 9:34 PM = 43.0 mm Hg
Po_2 (80.0-100.0)	5:45 PM = 94.8, 8:04 PM = 93.9, 9:34 PM = 58.2L mm Hg
Bicarbonate (20.0-24.0)	5:45 PM = 9.3L, 8:04 PM = 15.0, 9:34 PM = 17.7 mEq/L
Base (0.0-2.0)	5:45 PM = 22.8H, 8:04 PM= 13.9H, 9:34 PM = 9.6H
O_2 sat	5:45 PM = 90.4, 8:04 PM = 95.4, 9:34 PM = 88.2%
BNP - 6:28 pm	250.0H (0.0-100.0)
Rel. Ind.- 6:28 pm	3.3H (0.0-2.5)
Cortisol - 6:29 PM	35.9 (AM = 4.3-22.4 2g/dL, PM = 3.1-16.7 2g/dL)
PT - 6:28 pm	25.1 (11.6-15.2)
INR - 6:28 pm	2.3 (0.0-1.5)
PTT - 6:28 pm	63 (24-37)
Fibrinogen - 6:28 PM	153L (204-475 mg/dL)
D-Dimer - 6:28 PM	920.00 (0.00-0.48 ng/dL)
PLT - 6:28 pm	141L (150-400 2L)
K - 5:32 pm	3.2L (3.5-5.1 mEq/L)
CL - 5:32 pm	117H (96-112 mEq/L)
CO2 - 5:32 PM	16L (19-32 mm Hg)
Glucose - 5:32 PM	106H (70-99 mg/dL)
BUN - 5:32 pm	24H (6-23 mg/dL)
Crea - 5:32 pm	3.1H (0.4-1.2 mg/dL)
CA - 5:32 pm	7.3L (8.4-10.5 mg/dL)
TP - 5:32 pm	4.2L (6.0-8.3)
ALB - 5:32 pm	2.2L (3.5-5.2 g/dL)
AST - 5:32 pm	85H (0-37 U)
ALT - 5:32 pm	66H (0-40 U)
Lactic acid - 5:32 PM	10.6H (0.5-2.2), neutrophils 94H (43-77), Llymphocytes 51 (12-46), monocytes 1 L (3-11)
Amylase - 6:28 PM	441H (27-131)
Lipase - 6:28 PM	665H (22-51)
O2 content - 7:00 PM	47.9H (15.0-23.0)

Abbreviations: ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; CA, calcium; Cl, choloride; CO2, carbon dioxide; Crea, creatinine; HCT, hematocrit; HGB, hemoglobin; INR, international normalized ratio; K, potassium; Pco2, partial carbon dioxide level; PLT, platelet; Po2, partial oxygen level; PT, prothrombin time; PTT, partial thromboplastin time; Rel. Ind., relative index;

RBC, red blood cell count; TP, total protein; WBC, white blood cell count. H, indicated in some of the lab values indicates a HIGH value, according to the hospital’s standard lab values.

Pam's family came rushing into the unit. The looks on their faces revealed their fears. Her daughter was crying and being comforted by her brother. They were given a brief update and told that she had just arrived. They were reassured that as soon as we could get her situated, we would come out and get them. They were escorted by the unit secretary to the waiting area.

The team immediately began assessing Pam and obtaining her vital signs. She was tachycardic at 132 bpm. Her heart sounds were distant and regular without any ectopy. We could not get the arterial line to read a blood pressure. The only pressure that we could obtain was a faint Doppler blood pressure of 52. No one could palpate a peripheral pulse on any extremity. She did not have any capillary refill. She had generalized edema, and her skin was drawn so firm and tightly across her body that it was glossy in appearance.

Pam had no spontaneous respiratory effort. Her lung sounds were coarse crackles and rhonchi throughout. The team could not obtain a pulse oximetry reading on her because she was so cold to the touch. She was on 50% oxygen via ventilator. She did not have any bowel sounds. The Foley catheter that was in place had about 50 mL of very dark urine in it.

The team gave Pam 3 ampules of sodium bicarbonate IV push and began titrating her many drips in an effort to improve her physiological response to the therapy. She was on 180 mL/h of phenylephrine hydrochloride intravenous solution (Neo-Synephrine), 46.9 mL/h of norepinephrine bitartrate (Levophed), 6 mL/h of vasopressin, and 80 mL/h of dextrose 5% with bicarbonate. There was no response to these therapeutic interventions.

The phlebotomist came up from the laboratory, and the team drew multiple tubes of blood from the central venous catheter. Table 3 highlights the abnormal laboratory values. The family was anxiously waiting to see Pam and find out what was happening. Her brother and her 18-year-old twins, a boy and a girl, were nervously pacing in and out of the unit. We would race past them to get something else. Every member of the team took a minute here and there to give them a "there's no change" update report.

Table 3. Orders

2:57 PM	Rocephin 2 g IV PB
2:59 PM	ECG
3:00 PM	Chest AP portable
3:02 PM	Ice pack
3:30	NS wide open

PM	
4:29 PM	Chest AP portable
5:15 PM	Sepsis protocol, sedation protocol, ARDS protocol, hyperglycemia protocol, CBC, CMET, Ph, Mg, ABG, PT, PTT, cortisol, lactic acid, BNP, BAL, blood CX x 2, UA/C & S, DIC panel, pantoprazole (Protonix) 40 mg IV QD, PAS hose, Rocephin 2 g IV QD, doxycycline 100 mg IV every 12 h, NG to suction
5:30 PM	D/C Rocephin, vancomycin 1 g IV now, pharmacy to dose, imipenem and cilastatin (Primaxin) 500 mg IV now, pharmacy to dose, amylase and lipase, 2D echo, CBC, CMET, ABG, CXR am, cardiac enzymes with troponin q 8 x 3
6:09 PM	NS wide open
6:10 PM	Foley catheter
6:30 PM	D5W with 3 amps NaHCO3 at 80 mL/h, ABG at 8:00 PM
7:30 PM	Vancomycin 1 g IV 1 24 h, Primaxin 250 mg IV PB q 6 h
8:00 PM	2-L NS bolus now, STAT ABG, call MD with result and new CVP, UA, shave L groin, transfer to MICU for CVVHD, increase NaHCO3 gtt to 150 mL/h
8:07 PM	Fentanyl 100 mg IVP, Versed 4 mg IVP
8:13 PM	Increase vent rate to 32, decrease Fio_2 to 80% and wean, ABG 1/2 h
8:20 PM	Give 3 more amps bicarbonate now
9:16 PM	Transfuse 2 U FFP now
9:35 PM	Stool for fecal leukocytes, O & P
9:44 PM	Increase Fio_2 to 90%
12:30 AM	3 amps NaHCO3 now, 2 amps NaHCO3 IV q 15 min PRN for BP <75 x 2 h then call, CVVHD, keep SBP > 80 if possible, iSTAT

Abbreviations: 2D, 2-dimensional; ABG, arterial blood gas; Amps, ampules; AP, anterior/posterior; ARDS, adult respiratory distress syndrome; BAL, bronchoalveolar lavage; BNP, brain natriuretic peptide; BP, blood pressure; C & S, culture and sensitivity; CBC, complete blood count; CMET, complete metabolic test; CVP, central venous pressure; CVVDH, continous venovenous hemodialysis; CX, culture; CXR, chest x-ray; D/C, discharge; DIC, disseminated intravascular coagulation; Echo, echocardiogram; ECG, electrocardiogram; Fio2, percentage of inspired oxygen; IV PB, intravenous push bolus; MD, physician; Mg, magnesium; MICU, medical intensive care unit; NaHCO3, sodium bicarbonate; NG, nasogastric; NS, normal saline; PAS, pulsatile antiembolic sequential hose; PRN, as needed; PT, prothrombin time; PTT,

partial thromboplastin time; O&P, ova and parasites; SBP, systolic blood pressure; STAT, immediately; UA, urinalysis; Vent, ventilator.

At midnight, her drips had been increased to 210 mL/h of Neo-Synephrine and 46.9 mL/h of Levophed, and the vasopressin remained maxed out at 6 mL/h. Despite this, her vital signs continued to decline. Pam's heart rate was now at 132 bpm, and her blood pressure was now at 50 mm Hg via the Doppler. She seemed to be getting even colder and to be taking on a duskier and more cyanotic appearance. The physician remained with the team via the video monitoring system. The team discussed the available options and their potential to positively impact the patient's outcome.

By 12:15 AM, Pam's heart rate had dropped further, now down to 122 bpm, and her Doppler blood pressure was now almost undetectable. She was given 3 ampules of sodium bicarbonate since that had seemed to help previously, if only transiently.

The renal physician came in at 12:30 AM to evaluate Pam for the placement of a hemodialysis catheter for CRRT. He spoke only briefly with the family as Kristine hurriedly prepared the necessary supplies and consents for the procedure. He used a portable ultrasound to locate the femoral route he had chosen. It was a rough procedure because she had no blood pressure to assist with placement. Her heart rate was now down to 112 bpm.

Kristine explained to the family that the physician was going to try to get the dialysis catheter in place so that we could begin the CRRT. They said they understood. Kristine could see they were not listening at this point. They were grasping onto every piece of hope and courage they had.

At 12:45 AM, Pam's heart rate had dropped still further, now at 108 bpm. The team decided to try 2 more ampules of sodium bicarbonate. The team was now working at a maximum pace, having forgone the urgent phase and moved into the emergent phase. At 12:53 AM, she had no detectable pulse. The worst had happened; she developed pulseless electrical activity! A code blue was called, and within minutes, the room had filled with people.

The team worked as before, following all the protocols, using every drug, tool, and technique at our disposal. We worked long and hard for what seemed to be an eternity, but it was in actuality only 19 minutes. In the end, a 56-year-old woman's 29-hour battle for life had come to an end. Pam's devastated family and a stunned health care team were left standing in a room full of people, equipment, and knowledge but without answers for a family desperately seeking them. The question still unanswered was: "What happened? "

The protocol for management of septic shock that was in place in our facility, based on the guidelines of the Society of Critical Care Medicine,[1] had been instituted for this patient upon her arrival at the emergency department. Table 4shows the 2007 Sepsis Management and provides an outline of the septic shock protocol that we followed.[1] The team instituted all of the protocols

that we had: the sedation protocol, the adult respiratory distress syndrome protocol, and the hyperglycemia protocol.

Table 4. 2007 Sepsis Management[1]

Resuscitation	Supportive Care	Monitoring	Antibiotics
Airway	Vasopressors-norepi, dopa	Tissue perfusion	ID septic focus
Respirations	Phenylephrine	SBP >100	Blood CX x 2 before abx
Perfusion	Vasopressin	CVP 8-12	Empiric abx coverage
Restore BP to perfuse organs	Inotropes – dobutamine	Cardiac output	Vancomycin
Rapid, large volume, IV fluids	Glucose control; Nutritional support; Corticosteroids	MAP Q65; Svco2 Q70	3rd- or 4th-generation cephalosporin; β-Lactam/β-lactamase inhibitor no specific abx - general family of β lactames, etc, in addition to others; Carbapenem; Also drotrecogin α (Xigris)

Abbreviations: abx, antibiotic; BP, blood pressure; CVP, central venous pressure; CX, culture; dopa, dobutamine; ID, identify; IV, intravenous; MAP, mean arterial pressure; norepi, norepinephrine; SBP, systolic blood pressure; $Svco_2$, oxygen content.

Pam had received all of the "right" medications at the "right" time and at the "right" dosages. All of the appropriate medical consults had been made, and all of the recommended protocols were in place. Despite all of this, this 56-year-old woman died. Although she was with us only briefly, Pam had a huge impact on us. Even now Kristine thinks back to that time and wonders: "What if? "

SOLVING THE PUZZLE

The one unanswered question was: What was the offending agent? Exactly what had we all battled so long and hard to defeat? The autopsy report stated that the wound from her arm had grown *Streptococcus pyogenes*. A streptococcus infection, the same strain of streptococcus that causes necrotizing fasciitis in a dirty or infected wound, was the offending agent.

The autopsy report also stated that the pathologist had visited her home as a part of the autopsy investigation. He noted in the autopsy report: "Our autopsy technician and expert on spiders and snakes went out and visited with the family, obtaining a history of the patient's carrying lawn cuttings and debris to a compost pile, located in a different area of the yard, during which she noted the possible bite. In the area of the compost pile, some webs consistent with black spiders were identified as well as 3 black widow spiders, one of which had been caught by a family member."

BLACK WIDOW SPIDERS

Black widow spiders are 1 of 2 venomous domestic spiders found in North Carolina. The other is the brown recluse. The black widow spider, *Latrodectus mactans*, may be the most recognizable of the poisonous spiders because of the red "hourglass" shape on the abdomen of the female. This marking is found only on the female black widow.[2]

Black widow spiders are found in protected, dark spaces such as barns, under rocks or wooden boards, in garages, basements, and hollow stumps-anywhere it is damp and dark. They are not predatory in nature, but they will bite if disturbed or trapped.[2]

The venom of the female black widow is 15 times more potent than rattlesnake venom. This venom is a neurotoxin that alters the structure and function of the nerve terminals without producing any significant local reaction.[2] The toxin is [alpha]-latrotoxin. It is a protein that affects calcium metabolism at nerve terminals. There is a massive calcium uptake across plasma membranes, which causes a rapid and large release of acetylcholine, noradrenaline, dopamine, and [gamma]-aminobutyrate. Table 5 provides an outline of these effects of the neurotransmitters.[3-9]

Table 5. α-Latrotoxin Effects3-9

Acetylcholine	**Noradrenaline**	**Dopamine**	**γ- Aminobutyrate**
Transmits nerve impulses	Vasoconstrictor	Increases BP and urine output	Inhibits CNS
CNS and PNS	CNS	CNS and PNS	Dampening effect
Motor neuron	Fight or flight	Excitatory	
Parasympathetic	Sympathetic	Coordinate movements	Calms
Antagonizes dopamine	Smooth muscle relaxation	Regulates mood and emotions	Antagonizes dopamine
Skeletal muscles	Cardiac muscle contraction		

Abbreviations: BP, blood pressure; CNS, central nervous system; PNS, peripheral nervous system.

The bite might feel like a pinprick; however, the pain becomes intense shortly after. This pain spreads rapidly throughout the arms, legs, chest, back, and abdomen. This is accompanied by chills, vomiting, difficulty breathing and perfuse sweating, delirium, partial paralysis, violent abdominal cramping, and spasms.[2] These symptoms are similar to those reported by the patient to her family and to the EMS crew.

An elevation of the blood pressure and white blood cell counts will be noted. The bite area appears as a bluish red spot surrounded by a whitish area. This is similar to what was noted on examination of the patient, with the exception of the elevated white blood cell count. An antivenom serum is available, but it must be administered as soon as possible after the bite

occurs. Victims usually recover in 2 to 5 days; however, about 5% of all reported black widow attacks are fatal.[2]

The physiological effects that led to the Pam's demise were all related to the effects of [alpha]-latrotoxin, the neurotoxin in the black widow spider venom. The [alpha]-latrotoxin was responsible for an abnormal release of acetylcholine, leading to an increase in neuromuscular activity, which in turn caused muscle spasms and rigidity. This was followed by neuromuscular failure and paralysis. This in turn caused membrane depolarization and calcium influx throughout the body, which activated the calcium channels, adding to the influx of calcium. The activated calcium channels signaled a massive transmitter release and eventually depleted the stores of neurotransmitters.

In addition to the acetylcholine release, the [alpha]-latrotoxin from the black widow spider venom caused the release of noradrenaline, a potent vasoconstrictor in the central nervous system. The noradrenaline caused smooth muscle relaxation as well as cardiac muscle contraction, as evidenced by the patient's pulmonary collapse and tachycardia.

Dopamine is another neurotransmitter released as a result of the [alpha]-latrotoxin. The dopamine release had an excitatory effect on the central and peripheral nervous systems. The dopamine also contributed to the elevated blood pressure, tachycardia, and tachypnea initially seen in this patient.

The neurochemical [gamma]-aminobutyrate, also known as [gamma]-aminobutyric acid (GABA), is released as a result of the [alpha]-latrotoxin effects on the human body. The [gamma]-aminobutyrate, or GABA, also affects the central nervous system, although it has an inhibitory effect and antagonizes dopamine. Now the body is fighting itself as these potent neurotransmitters battle it out for control.

All of these neurotransmitters are pieces of a very complex network of reactions that are dependent upon each other for harmony within this delicate chemical system. When something disrupts the harmony, the entire network of neurotransmitter reactions is interrupted. This, in turn, disrupts the physiological and pathophysiological responses within the human body. When this happens, the body systems no longer respond in their normal fashion, because their chemical signals have altered their responses.

When the body might normally have an increased body temperature as a result of a detected threat or insult, the body will instead have a decreased body temperature as a result of the misaligned chemical signaling. Thus, what may be an unexpected response becomes the expected response of this body in disarray. Because both the central and peripheral nervous systems are affected by this neurotoxin, we could expect to see wild swings in the body's responses. Thus, in the patient with the black widow spider bite, there was an elevated blood pressure followed by a rapid drop in blood pressure, or a tachycardia followed by a bradycardia.

Pam's clinical manifestations were consistent with those described above. At first, her vital signs were mildly elevated, as would be expected as a result of the release of dopamine and noradrenaline. This was followed by an extreme elevation, most probably due to the increasing levels of dopamine and noradrenaline being released as her body went into a survival, fight-or-flight mode. Then a rapid decline of her vital signs followed, probably due to the competing neurotransmitters and calcium ion fluctuation, predominately GABA and acetylcholine, as these levels continued to rise and the dopamine and noradrenaline levels began to fall because of depletion of available stores.

These presenting signs appear much like a shock state. Thus, this patient was treated with the most current treatments for septic shock, guided by the Society of Critical Care Medicine's guidelines.[1] The first step in this treatment phase is volume resuscitation, with the goals of a central venous pressure (CVP) of 8 to 12 mm Hg, a mean arterial pressure of 65 mm Hg or greater, urine output equal to or greater than 0.5 mL/kg per hour, and a central venous oxygen saturation of 70% or greater. The fluid resuscitation should continue for the first 6 hours, with fluid challenges of 1000 mL of crystalloids over 30 minutes given on an hourly basis, as needed, based on the parameters. This patient's CVP never got into the "normal" range of 8 to 12 mm Hg. Hers was never higher than 6 mm Hg, when we could get the CVP line to read.

The next phase of septic shock treatment calls for obtaining 2 blood cultures and beginning broad-spectrum antibiotic treatment until the offending agent(s) is identified. After this, usually within an hour, if the fluid resuscitation is not showing any improvement, vasopressors are administered.

Norepinephrine and dopamine are the initial vasopressors of choice, administered via a central access, for the mean arterial pressure goal. This patient had these 2 drugs running at the maximum doses, without effect. As one might expect, because the [alpha]-latrotoxin was still affecting her neurotoxin levels, the effects of what we were putting in were being blunted by the elevated levels of acetylcholine and GABA and therefore not having the positive effects we were looking for.

Pam was also given IV hydrocortisone based on the protocol, which is given when hypotension responds poorly to resuscitation and vasopressors. Vasopressin 0.03 U/min was added next in the process. This is the maximum dose for vasopressin; it is not titrated up or down as other vasopressors are. Vasopressin is meant to aid the effects of the norepinephrine. Again, with this patient, had we known that the acetylcholine and GABA were blunting what we were trying to do, we might have been able to achieve a more positive outcome.

A mere 29 hours earlier, Pam was going about her life, fairly healthy and working in her garden. She received a bite of some kind and became profoundly septic and succumbed. If we had known then what we found out later, would that have changed the outcome? If a black widow

spider bite was the offending agent, and she had received the antivenom, could we have changed the outcome?

LESSONS AND QUESTIONS

We cannot always expect to know, or discover, everything about our patients when they arrive at our doorsteps in a critically ill state. Not every case will have an answer, even after the fact. However, events such as the one reported here raise the question, is it not worth a few extra minutes of investigatory questioning to solve the riddle? This event should be a reminder of the importance of obtaining a detailed patient history. Learning to hone in on the unanswered questions and digging a little deeper may make the difference in the outcome. There were many opportunities in this case for additional investigation.

Kristine remembers Pam so clearly, even now, because it seemed as though we were fighting an uphill battle against an unknown enemy. Despite all that was tried, based on our knowledge, we were not successful. Kristine could not help wondering afterward: If only we had known what was causing her symptoms, perhaps we could have had a more positive outcome.

The patient did not and perhaps could not respond, despite maximum septic shock treatment, fluid resuscitation, and antibiotic therapy, because of the elevated levels of the various neurotoxins and their actions and counteractions. Did the vasopressors that we gave her make things worse? Did the administration of these inadvertently create a situation in which levels just continued to get higher and higher and got so far out of control that they were beyond our reach? Did all the dopamine and norepinephrine cause an increase in GABA and acetylcholine? Did the added vasopressin contribute to this effect?

We will never know all of the answers to these questions. Every patient is different, but each one has something to teach us about the physiology and pathophysiology of his/her illness. We must continue to ask questions, seek answers, and share the lessons learned. Through this learning journey, we all can gain new knowledge, which can then be used to help others.

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